

WHAT IS CLAIMED IS:

1. An antibody that binds specifically to a polypeptide comprising an ubiquitination-regulating domain.
2. The antibody of claim 1, wherein said ubiquitination-regulating domain is an ubiquitination-regulating domain, or a functional fragment thereof, of a TSG101 protein.
3. The antibody of claim 2, wherein said TSG101 protein is a human TSG101 protein.
4. The antibody of claim 3, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of said human TSG101 protein.
5. The antibody of claim 3, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of said human TSG101 protein.
6. The antibody of claim 3, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of said human TSG101 protein.
7. A method of producing an antibody that binds specifically to an ubiquitination-regulating domain, comprising raising said antibody against a polypeptide comprising said ubiquitination-regulating domain.
8. The method of claim 7, wherein said ubiquitination-regulating domain is a ubiquitination-regulating domain, or a functional fragment thereof, of a TSG101 protein.
9. The method of claim 8, wherein said TSG101 protein is a human TSG101 protein.
10. The method of claim 9, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of said human TSG101 protein.

11. The method of claim 8, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of said human TSG101 protein.

12. The method of claim 9, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of said human TSG101 protein.

13. A method of treating a condition in a subject, said condition resulting from a change in a level of MDM2 protein in cells of said subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent comprising an ubiquitination-regulating domain.

14. A method of treating a condition in a subject, said condition resulting from a change in a level of a TSG101 protein in cells of said subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent modulating the interaction of said TSG101 protein with MDM2.

15. A method for treatment of a proliferative disease in a subject comprising:

- (a) monitoring the subject for a level of p53; and
- (b) treating the subject with an agent so as to maintain said level of p53 within a target range, wherein said agent comprises an ubiquitination-regulating domain.

16. A method for treatment of a proliferative disease in a subject comprising:

- (a) monitoring the subject for a level of TSG101; and
- (b) treating the subject with an agent so as to maintain said level of TSG101 within a target range, wherein said agent modulates the interaction of said TSG101 with MDM2.

17. The method of claim 13, 14, 15 or 16, wherein said ubiquitination-regulating domain is an ubiquitination-regulating domain, or a functional fragment thereof, of a TSG101 protein.

18. The method of claim 17, wherein said TSG101 protein is a human TSG101 protein.

19. The method of claim 18, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of said human TSG101 protein.

20. The method of claim 18, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of said human TSG101 protein.

21. The method of claim 18, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of said human TSG101 protein.

22. A method for treating a proliferative disease in a subject, said method comprising administering to said subject a therapeutically effective amount of an agent, said agent modulating the interaction of a TSG101 protein with MDM2.

23. A cell comprising a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence such that said cell expresses said ubiquitination-regulating domain.

24. A cell comprising (i) a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence; and (ii) a polynucleotide encoding MDM2 protein operationally linked to a regulatory sequence, such that said cell expresses said ubiquitination-regulating domain and said MDM2 protein.

25. A cell comprising (i) a polynucleotide encoding an ubiquitination-regulating domain operationally linked to a regulatory sequence; (ii) a polynucleotide encoding

MDM2 protein operationally linked to a regulatory sequence; and (iii) a polynucleotide encoding p53 protein operationally linked to a regulatory sequence, such that said cell expresses said ubiquitination-regulating domain, said MDM2 protein, and said p53 protein.

26. The cell of claim 23, 24 or 25, wherein said ubiquitination-regulating domain is an ubiquitination-regulating domain, or a functional fragment thereof, of a TSG101 protein.

27. The cell of claim 26, wherein said TSG101 protein is a human TSG101 protein.

28. The cell of claim 27, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of said human TSG101 protein.

29. The cell of claim 27, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of said human TSG101 protein.

30. The cell of claim 27, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of said human TSG101 protein.

31. A method of identifying an agent that modulates the interaction of a TSG101 protein with MDM2, comprising screening candidate agents using a screening assay comprising a cell expressing MDM2 and a polypeptide comprising an ubiquitination-regulating domain, or a functional fragment thereof, of said TSG101 protein.

32. A method of identifying an agent that is capable of modulating the interaction of a TSG101 protein with MDM2, comprising:

- (a) contacting a first cell expressing MDM2 and a polypeptide comprising an ubiquitination-regulating domain, or a functional fragment thereof, of

said TSG101 protein with said agent and measuring MDM2 level in said first cell;

(b) contacting a second cell expressing MDM2 but not an ubiquitination-regulating domain, or a functional fragment thereof, of said TSG101 protein, with said agent and measuring MDM2 level in said second cell; and

(c) comparing MDM2 levels measured in (a) and (b),

wherein a difference in MDM2 levels compared in step (c) identifies said agent as capable of modulating the interaction of the TSG101 protein with MDM2.

33. The method of claim 31 or 32, wherein said TSG101 protein is a human TSG101 protein.

34. The method of claim 33, wherein said ubiquitination-regulating domain comprises amino acid residues 50-140 of said human TSG101 protein.

35. The method of claim 33, wherein said ubiquitination-regulating domain comprises amino acid residues 1-140 of said human TSG101 protein.

36. The method of claim 33, wherein said ubiquitination-regulating domain comprises amino acid residues 140-250 of said human TSG101 protein.

37. A method of modulating a level of MDM2 in a cell, comprising contacting said cell with a polypeptide or derivative thereof that comprises a polypeptide comprising an ubiquitination-regulating domain.

38. A method of modulating a level of p53 in a cell, comprising contacting said cell with a polypeptide or derivative thereof that comprises a polypeptide comprising an ubiquitination-regulating domain.

39. A method of modulating a level of TSG101 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG101 protein with MDM2.

40. A method of modulating a level of MDM2 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG101 protein with MDM2.

41. A method of modulating a level of p53 in a cell, comprising contacting said cell with an agent that is capable of modulating the interaction of a TSG101 protein with MDM2.

42. A method for screening for a cellular protein that interacts with an ubiquitination-regulating domain, comprising identifying a cellular protein that binds said ubiquitination-regulating domain.